UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,172	02/12/2004	Stephen D. Wolpe	1331-413	4014

23117 7590 10/05/2004

NIXON & VANDERHYE, PC
1100 N GLEBE ROAD
8TH FLOOR
ARLINGTON, VA 22201-4714

EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/776,172	WOLPE ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-90* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-90 are pending.

Restriction Requirement

It is noted that:

(i) claim 40 recites the apparent typographical error of " a method of claim 39". This phrase is being interpreted as "the pharmaceutical composition of claim 39" for the purpose of restriction;

(ii) claim 42 recites the apparent typographical error of " a method of claim 41". This phrase is being interpreted as "the pharmaceutical composition of claim 41" for the purpose of restriction.

(iii) Claims 89-90 on pages 125-126 of the specification were originally incorrectly numbered as claims 87-88. In accordance with 37 CFR 1.126, claims 87-88, second occurrence have been renumbering as claims 89-90. Accordingly, for the purposes of restriction, dependent renumbered claim 90 is being interpreted as being dependent upon renumbered claim 89.

2. Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-8 , drawn to a polypeptide comprising hemoglobin alpha chain and a pharmaceutical composition comprising said polypeptide, classified in Class 424, subclass 185.1 and Class 530, subclass 385.

II. Claims 9-10, drawn to a method of inhibiting stem cells proliferation, comprising contacting said cells with a polypeptide comprising hemoglobin alpha chain classified in Class 435, subclass 375

III. Claim 11, drawn to a method of stimulating the growth of B cells , comprising contacting said cells with a polypeptide comprising hemoglobin alpha chain classified in Class 435, subclass 375

IV. Claims 12-16, drawn to a method of treating cancer in a mammal comprising administering , a polypeptide comprising hemoglobin alpha chain classified in Class 424, subclass 185.1.

V. Claims 17-18 , drawn to a method of treating cancer in a mammal comprising treating hematopoietic cells ex vivo with a polypeptide comprising hemoglobin alpha chain and transplanting said treated cells into said mammal classified in Class 424, subclass 577.

VI. Claims 19-21 , drawn to a method of inhibiting stem cell division, in a mammal comprising administering an inhibiting amount of a polypeptide comprising hemoglobin alpha chain, classified in Class 424, subclass 577.

VII. Claims 22-24, drawn to a method of maintaining hematopoietic stem cell *ex vivo*, comprising contacting said cells with an inhibiting amount of a polypeptide comprising hemoglobin alpha chain , classified in Class 435, subclass 374.

VIII. Claims 25-26 , drawn to a method of treating a myeloproliferative disease comprising administering of a polypeptide comprising hemoglobin alpha chain classified in Class 424, subclass 185.1.

IX. Claim 25 , drawn to a method of treating a autoimmune disease comprising administering of a polypeptide comprising hemoglobin alpha chain classified in Class 424, subclass 185.1.

X. Claim 25 , drawn to a method of treating epithelial stem cell hyperproliferation disease comprising administering of a polypeptide comprising hemoglobin alpha chain classified in Class 424, subclass 185.1.

XI. Claims 27-29 , drawn to a method of differentially protecting normal stem cells and not cancer cells in mammal comprising administering a protective amount of a polypeptide comprising hemoglobin alpha chain classified in Class 424, subclass 185.1.

XII. Claim 30 , drawn to a method of vaccinating a mammal comprising administering a polypeptide comprising hemoglobin alpha chain classified in Class 424, subclass 185.1.

XIII. Claim 31 , drawn to a method of treating a mammal having immunodepression comprising administering of a polypeptide comprising hemoglobin alpha chain classified in Class 424, subclass 185.1.

XIV. Claims 32-35 , drawn to a method of conducting gene therapy in a mammal classified in Class 424, subclass 577.

XV. Claims 36-38 , drawn to a method for conducting *ex vivo* stem cell expansion, comprising contacting said cells with a polypeptide comprising hemoglobin alpha chain classified in Class 435, subclass 375.

XVI. Claims 39 and 40 , drawn to a pharmaceutical composition comprising a polypeptide comprising hemoglobin alpha chain and at least one inhibitory compound , classified in Class 424, subclass 185.1 and 85.1

XVII. Claims 41 and 42 , drawn to a pharmaceutical composition comprising a polypeptide comprising hemoglobin alpha chain and at least one stimulatory compound , classified in Class 424, subclass 185.1 and 85.2.

XVIII. Claims 43-45 , drawn to a method for expressing alpha hemoglobin or substitution or deletion analogs thereof , classified in Class 435, subclass 85.2.

XIX. Claim 46 , drawn to a peptide having the sequence recited in claim 46 , classified in Class 530, subclass 300.

XX. Claims 47-50, drawn to a method of stimulating stem cell proliferation , comprising contacting said cells with a INPROL **and** opiate compound classified in Class 435, subclass 375.

XXI. Claims 47-49, drawn to a method of stimulating stem cell proliferation , comprising contacting said cells with a INPROL , classified in Class 435, subclass 375.

XXII. Claims 47 and 50 drawn to a method of stimulating stem cell proliferation , comprising contacting said cells with a opiate compound , classified in Class 435, subclass 375.

XXIII. Claims 51-52, drawn to a method of stimulating stem cell proliferation , comprising contacting said cells with a compound capable of binding to opiate receptor , classified in Class 435, subclass 375.

XXIV. Claim 53 , drawn to a method of stimulating stem cell proliferation , comprising contacting said cells with a compound capable of binding to nociceptin receptor , classified in Class 435, subclass 375.

XXV. Claim 53 , drawn to a method of inhibiting stem cell proliferation , comprising contacting said cells with a compound capable of binding to nociceptin receptor , classified in Class 435, subclass 375.

XXVI. Claim 53 , drawn to a method of stimulating stem cell proliferation , comprising contacting said cells with a compound capable of binding to $G_{\text{inhibitory}}$ subclass of GTP binding proteins , classified in Class 435, subclass 375.

XXVII. Claim 53 , drawn to a method of inhibiting stem cell proliferation , comprising contacting said cells with a compound capable of binding to $G_{inhibitory}$ subclass of GTP binding proteins , classified in Class 435, subclass 375.

XXVIII. Claims 55-57 , drawn to a method of stimulating stem cell proliferation , comprising contacting said cells with a compound capable of binding to opiate-like receptor , classified in Class 435, subclass 375.

XXIX. Claims 55-57 , drawn to a method of inhibiting stem cell proliferation , comprising contacting said cells with a compound capable of binding to opiate-like receptor , classified in Class 435, subclass 375.

XXX. Claims 58-59 , drawn to a method of identifying a receptor for INPROL in a receptor-binding assay , classified in Class 435, subclass 7.1.

XXXI. Claims 60-61 , drawn to a method of identifying a receptor for INPROL in a adenylate cyclase assay , classified in Class 435, subclass 7.2

XXXII. Claims 62-65 , drawn to a method of treating cancer in a mammal comprising administering , INPROL **and** opiate compound classified in Class 424, subclass 185.1.

XXXIII. Claims 62-64 , drawn to a method of treating cancer in a mammal comprising administering INPROL in Class 424, subclass 185.1.

XXXIV. Claims 62-65 , drawn to a method of treating cancer in a mammal comprising administering opiate compound classified in Class 424, subclass 185.1.

XXXV. Claims 66-68 , drawn to a method of stimulating stem cell division in a mammal comprising administering , INPROL **and** opiate compound classified in Class 424, subclass 185.1.

XXXVI. Claims 66-67 , drawn to a method of stimulating stem cell division in a mammal comprising administering INPROL classified in Class 424, subclass 185.1.

XXXVII. Claims 66-68 , drawn to a method of stimulating stem cell division in a mammal comprising administering opiate compound classified in Class 424, subclass 185.1.

XXXVIII. Claims 69-71 , drawn to a method of maintaining hematopoietic stem cells ex-vivo comprising contacting said cells with INPROL **and** opiate compound classified in Class 435, subclass 373.

XXXIX. Claims 69-70 , drawn to a method of maintaining hematopoietic stem cells ex-vivo comprising contacting said cells with INPROL classified in Class 435, subclass 373.

XL. Claims 69-71 , drawn to a method of maintaining hematopoietic stem cells ex-vivo comprising contacting said cells with opiate compound classified in Class 435, subclass 373.

XLI. Claims 72-74 , drawn to a method of treating a myeloproliferative disease comprising administering of INPROL **and** opiate compound classified in Class 424, subclass 185.1.

XLII. Claims 72-73 , drawn to a method of treating a myeloproliferative disease comprising administering of INPROL classified in Class 424, subclass 185.1.

XLII. Claims 72-74 , drawn to a method of treating a myeloproliferative disease comprising administering of opiate compound classified in Class 424, subclass 185.1.

XLIII. Claims 72, 74 , drawn to a method of treating a hematopoietic or epithelial stem cell hyperproliferation comprising administering of INPROL **and** opiate compound classified in Class 424, subclass 185.1.

XLIV. Claim 72, drawn to a method of treating a hematopoietic or epithelial stem cell hyperproliferation comprising administering of INPROL classified in Class 424, subclass 185.1.

XLV. Claims 72, 74 , drawn to a method of treating a hematopoietic or epithelial stem cell hyperproliferation comprising administering of opiate compound classified in Class 424, subclass 185.1.

XLVI. Claims 75-77 , drawn to a method for treating or preventing stem cell exhaustion, comprising administering of INPROL **and** opiate compound classified in Class 424, subclass 185.1.

XLVII. Claims 75 and 76 , drawn to a method for treating or preventing stem cell exhaustion comprising administering of INPROL classified in Class 424, subclass 185.1.

XLVIII. Claims 75-77 , drawn a method for treating or preventing stem cell exhaustion comprising administering of opiate compound classified in Class 424, subclass 185.1.

XLIX. Claims 78-79 , drawn a method for differentially protecting normal stem cells in a mammal comprising administering of opiate compound classified in Class 424, subclass 185.1.

L. Claims 80-81 , drawn a method of conducting gene therapy in a mammal comprising treating hematopoietic cells with stimulatory amount of INPROL **and** opiate compound classified in Class 424, subclass 185.1.

LI. Claims 80 , drawn a method of conducting gene therapy in a mammal comprising treating hematopoietic cells with stimulatory amount of INPROL classified in Class 424, subclass 185.1.

LII. Claims 80-81 , drawn a method of conducting gene therapy in a mammal comprising treating hematopoietic cells with stimulatory amount of opiate compound classified in Class 424, subclass 185.1.

LIII. Claims 82-84 , drawn a method of conducting ex vivo stem cell expansion comprising contacting hematopoietic cells with stimulatory amount of INPROL **and** opiate compound classified in Class 435, subclass 375.

LIV. Claims 82-83 , drawn a method of conducting ex vivo stem cell expansion comprising contacting hematopoietic cells with stimulatory amount of INPROL classified in Class 435, subclass 375.

LV. Claims 82-84 , drawn a method of conducting ex vivo stem cell expansion comprising contacting hematopoietic cells with stimulatory amount of opiate compound classified in Class 435, subclass 375.

LVI. Claim 85 , drawn a pharmaceutical composition comprising an opiate compound and at least one inhibitory compound, classified in Class 424, subclass 185.1 and 85.1.

LVII. Claim 86 , drawn a pharmaceutical composition comprising an opiate compound and at least one stimulatory compound compound, classified in Class 424, subclass 185.1 and 85.2.

LVIII. Claims 87 and 88 , drawn to a method for treating pain in a mammal comprising administering of INPROL classified in Class 424, subclass 185.1.

LIX. Claims 89-90 , drawn to a method for treating immune deficiency in a mammal comprising administering of INPROL classified in Class 424, subclass 185.1.

3. Groups II-XV, XVIII, XX-LV, LVIII and LIX are different methods. These inventions are different with respect to ingredients, method steps, and endpoints which require non-coextensive searches ; therefore, each method is patentably distinct.

4. Groups I, XVI, XVII, XIX, LVI and LVII are different products. These inventions are differ with respect to their structures and physicochemical properties and mode of action, which require non-coextensive searches; therefore each product is patentably distinct.

5 Groups I and II-XV ; XIX and XX-L are related as product and process of using. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptides of Groups I and XIX can be used for crystallography in addition to the recited methods.

6. These inventions are distinct for the reasons given above. In addition, they have acquired a separate status in the art as shown by different classification and/or recognized divergent subject matter. Further, even though in some cases the classification is shared, a different field of search would be required based upon the structurally distinct products recited and the various methods of use comprising distinct method steps. Moreover, a prior art search also requires a literature search. It is an undue burden for the examiner to search more than one invention. Therefore restriction for examination purposes as indicated is proper.

Species Election

Applicant is further required under 35 USC 121 (1) to elect a single disclosed species to which the claims would be restricted if no generic claim is finally held to be allowable and (2) to list all claims readable thereon including those subsequently added.

7. If Group XVI is elected, applicant is required to elect a specific pharmaceutical composition wherein one specific inhibitory compound is selected from the group recited in claim 39.

These species are distinct because their structure, physicochemical properties and mode of action are different. The examination of species would require different searches in the scientific literature.

8. If Group XVII is elected, applicant is required to elect a specific pharmaceutical composition wherein one specific stimulatory compound is selected from the group recited in claim 41.

These species are distinct because their structure, physicochemical properties and mode of action are different. The examination of species would require different searches in the scientific literature.

9. If Group XIX is elected, applicant is required to elect a specific peptide wherein one specific peptide is selected from the group recited in claim 46.

These species are distinct because their structure, physicochemical properties and mode of action are different. The examination of species would require different searches in the scientific literature.

10. If any of Group XX-XXII, XXXII, XXXIV, XXXV,XXXVII, XXXVIII, XL, XLI, XLII, XLVI, XLVIII, XLIX, L, LII is elected, applicant is required to elect a specific method wherein one specific INPROL peptide is selected from the group recited in claim 49 and one specific opiate compound is selected from the group recited in claims 50, 65, 68, 71, 74, 77, 79, 81,

These species are distinct because a specific method wherein one specific INPROL peptide is selected from the group recited in claim 49 and one specific opiate compound is selected from the group recited in claim 50, 65, 68, 71, 74, 77, 79, 81, differ with respect to the specific INPROL peptide and specific opiate compound; thus each specific method employing a specific INPROL peptide and specific opiate compound represents patentably distinct subject matter. The examination of species would require different searches in the scientific literature.

11. If any one of Group XXX or XXXI is elected, applicant is required to elect a specific method of identifying a receptor for INPROL, wherein one specific INPROL is selected from the group recited in claim 59 or 61.

These species are distinct because the a specific method of identifying a receptor for INPROL, wherein one specific INPROL is selected from the group recited in claim 59 or 61 differ with respect to the specific INPROL peptide thus each specific method employing a specific INPROL peptide represents patentably distinct subject matter. The examination of species would require different searches in the scientific literature.

12. If Group LVI is elected, applicant is required to elect a specific pharmaceutical composition wherein one specific inhibitory component is selected from the group recited in claim 85.

These species are distinct because their structure, physicochemical properties and mode of action are different. The examination of species would require different searches in the scientific literature.

13. If Group LVII is elected, applicant is required to elect a specific pharmaceutical composition wherein one specific stimulatory component is selected from the group recited in claim 86.

These species are distinct because their structure, physicochemical properties and mode of action are different. The examination of species would require different searches in the scientific literature.

14. If any one of the Groups LVIII or LIX is elected, applicant is required to elect a specific method , wherein a specific INPROL is selected from the group recited in claim 89 or 90.

These species are distinct because a specific method wherein one specific INPROL peptide is selected from the group recited in 89 or 90 differ with respect to the specific INPROL peptide thus each specific method employing a specific INPROL peptide represents patentably distinct subject matter. The examination of species would require different searches in the scientific literature

15. Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. § 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. M.P.E.P. § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

16. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

17. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

A telephone call was made to Gary Tanigawa on 09/28/04 to request an oral election to the above restriction requirement, but did not result in an election being made.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
September 28, 2004

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600